REMARKS

Claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, and 139-163 are pending in the present application. Claims 2, 5-7, 9-11, 17-18, 20, 22, 25, 27-28, and 30-138 have previously been cancelled without prejudice or disclaimer.

Claims 1 and 21 have been amended to require, in part, that the propylene glycol be present "...in an amount of less than 5% by weight..." and that the "...pH of the final product is in the range of from 5.0 to 7.0..." Also, new claims 162 and 163 have been added to recite that the pharmaceutical compositions of claim 1 and claim 21 are "...free of propylene glycol."

Support for the amendments and new claims appears throughout the specification and claims as originally filed. No new matter has been added. Applicants, by amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any claim. Applicants reserve the right to reassert any of the claims canceled or the original claim scope of any claim amended herein, in a continuing application.

In view of the following, further and favorable consideration is respectfully requested.

OBVIOUSNESS REJECTIONS

A. At page 3 of the Official Action, claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, 139, 141-144, 146-151, and 153-160 have been rejected under 35 USC § 103 (a), as being unpatentable over Peck et al. in view of Yu et al.

B. At page 9 of the Official Action, claims 140, 145, 152, and 161 have been rejected under 35 USC § 103 (a), as being unpatentable over Peck et al. in view of Yu et al., and further in view of Uchikawa et al.

Regarding rejection **A**, the Examiner asserts that "…it would have been obvious to one of ordinary skill in that the art at the time the invention was made [to] combine the teachings of Peck and Yu et al. and utilize the instant acid" because "Yu teaches adding lactic acid dissolves minoxidil providing better penetration of minoxidil. Therefore, a skilled artisan would have been motivated to add an acid to form a minoxidil acid salt for enhanced penetration of minoxidil into the hair follicle."

Specifically, Peck teaches quick breaking foams comprising, *inter* alia, 1-5% minoxidil and 10-50% propylene glycol.

Yu teaches, *inter alia*, a solution containing 2% minoxidil, 3% lactic acid, 80% ethanol and 15% propylene glycol, and a pH of 4.7 in Example 3.

Regarding rejection **B**, the Examiner asserts that it would have been obvious to the skilled artisan "to combine the teachings of the above references and substitute the exemplified propylene glycol with the instantly claimed glycerol and arrive at the instant invention" because "Uchikawa teaches both propylene glycol and glycerol are polyhydric alcohols conventionally used in the art."

Applicants maintain their traversal of these rejections.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *See KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

With regard to both rejections **A** and **B**, Applicants respectfully submit that the

teachings of Peck in view of both Yu alone and Yu and Uchikawa are primarily directed to compositions containing low minoxidil amounts (1-5% in Peck and 2% in Yu) in combination with high propylene glycol amounts (10-50% in Peck and 15% in Yu).

In contrast, the instantly claimed subject matter is directed to high amounts of minoxidil ("at least 5%" according to claim 1) and little to no propylene glycol ("less than 5%" according to claims 1 and 21 and none according to claims 162 and 163). These claimed amounts of propylene glycol are not recognized, disclosed or taught in any of the cited references as required by *In re Wilson*. Further, Applicants respectfully submit that the skilled artisan would not have looked to the teachings of Peck in view of Yu alone or in further combination with Uchikawa in order to arrive at the instant subject matter because these references teach low amounts of minoxidil in combination with high amounts of propylene glycol. The cited references do not provide any motivation to increase the amount of minoxidil and decrease the amount of propylene glycol. Thus, the cited references fail to render the instantly claimed subject matter obvious.

Further, Applicants submit that the cited references, when combined, do not provide a reasonable expectation of success based upon the fact the references teach high levels of propylene glycol. Peck broadly describes at page 2 a composition (1) that includes 1 to about 5% minoxidil and 10 to about 50% propylene glycol. Thereafter, Peck describes specific formulations, for example,

formulations (e) and (f) at page 4, that each include 50% propylene glycol and 5% minoxidil. Further, each of Examples 5 and 6 of Peck describe preparing compositions including 5% minoxidil and 50% propylene glycol.

The formulations of Peck that include a high concentration of minoxidil, i.e., 5%, also include high concentrations of propylene glycol, i.e., 50%. *See* formulations (e) and (f), and Examples 5 and 6.

Moreover, all of the examples of Peck have very ***high levels*** of propylene glycol or other diols and triols. Peck describes a composition that includes 1 to about 5% minoxidil and 10 to about 50% propylene glycol. Peck does ***not*** describe or exemplify a composition containing ***both*** at least 5% minoxidil and less than 5% propylene glycol.

The description in Peck of a composition that includes 1 to about 5% minoxidil and 10 to about 50% propylene glycol does not provide any motivation to modify the compositions described therein and arrive at the presently claimed compositions, i.e., at least 5% minoxidil and less than 5% propylene glycol. In fact, the cited references teach away from decreasing the amount of propylene glycol present to arrive at the presently claimed compositions, since the cited references specifically teach using high amounts of propylene glycol in combination with 5% of minoxidil. Specifically, Peck describes, at page 2, composition (1) that includes 1 to about 5% minoxidil and 10 to about 50% propylene glycol. Thereafter, Peck describes specific formulations, for example, formulations (e) and (f) at page 4, that

each includes 50% propylene glycol and 5% minoxidil. Further, each of Examples 5 and 6 of Peck describes preparing compositions including 5% minoxidil and 50% propylene glycol. Peck do not describe, let alone exemplify, a composition containing at least 5% minoxidil or a pharmaceutically acceptable salt thereof ***AND*** less than 10% by weight propylene glycol, ***let alone less than 5% by weight propylene glycol as is presently claimed***.

Moreover, all of the examples of Peck have very ***high levels*** of propylene glycol or other diols and triols. This is conventional technology that uses high propylene glycol concentrations in order to load minoxidil into the formulation. In Example 1, where the propylene glycol amount is 20%, there is only 2% minoxidil in the formulation. In Example 2(a), where propylene glycol and butylene glycol are present in a combined amount of 40%, there is only 2% minoxidil. In Example 2 (b), where the butylene glycol amount is 15%, there is only 1% minoxidil. Likewise, in Examples 3 and 4, where the propylene glycol amount is 30%, there is only 2% minoxidil in the formulation. In Example 7, where propylene glycol and butylene glycol are present in a combined amount of 25%, there is only 2% minoxidil. Only in Examples 5 and 6 where the propylene glycol amount is 50%, is minoxidil present in an amount of 5% in the formulations. This does not teach or suggest an advantage of having ***BOTH*** **reduced levels** of the co-solvent such as less than 5% propylene glycol and **high loading of minoxidil** such as at least 5%, as is presently claimed. Accordingly, Peck does not teach or suggest the presently claimed subject matter.

The foregoing remarks are further supported by the previously submitted Declaration under 37 CFR §1.132 by Barry Hunt ("the Hunt Declaration", submitted November 8, 2007), as well as the arguments made in previous responses to Office Actions in this application. Barry Hunt is a formulation scientist of the assignee of the subject application and has been in pharmaceutical research since 1972. He has been employed doing formulation research and development for the last 35 years.

In paragraphs 4-8, Mr. Hunt declares that he reviewed Peck and, as exemplified therein, formulations having high loading of minoxidil are accompanied by high levels of polyhydric alcohols. In fact, in paragraph 8, Mr. Hunt sets forth that Peck exemplify the following formulations:

- The composition of Example 5 contains 5% minoxidil and 50% propylene glycol.
- The composition of Example 6 contains 5% minoxidil and 50% propylene glycol.
- Compositions (e) and (f) each contain 5.0% minoxidil and 50.0% propylene glycol.
- The compositions of claims 13 and 14 each contain 5.0% minoxidil and 50.0% propylene glycol.

Thus, Mr. Hunt declares in paragraph 8 that, similar to other compositions described in the prior art, the compositions exemplified in Peck contain a very high percentage (i.e., 50%) of propylene glycol in order to improve the solubility of a high concentration (i.e. 5%) of minoxidil. Such high amounts of propylene glycol are not

pharmaceutically or cosmetically elegant, may be unacceptable to the consumer, and may cause local irritation and hypersensitivity upon application to the scalp (*see* paragraph 6 of the Hunt Declaration).

With specific regard to Yu, Yu does not cure the deficiencies of Peck because Yu also does not teach or suggest a composition having ***BOTH*** at least 5% minoxidil or a pharmaceutically acceptable salt thereof ***AND*** less than approximately 5% by weight polyhydric alcohol. Yu is directed to the use of hydroxyacids to enhance the "therapeutic efficacy of cosmetic and pharmaceutical agents." *See* col. 2, lines 16-21. In particular, Yu describes the use of "hydroxycarboxylic acids and related compounds" as "enhancing compounds" to enhance the therapeutic efficacy of cosmetic and pharmaceutical agents in topical treatment of cosmetic conditions, dermatologic disorders, or other afflictions. *See* col. 2, lines 16-42.

Yu clearly do not describe or suggest the present compositions which require "at least 5% by weight, based on the total weight of the composition, of minoxidil or a pharmaceutically acceptable salt thereof," "an acid in an amount to substantially completely solubilize the minoxidil or a pharmaceutically acceptable salt thereof," and a co-solvent wherein when the co-solvent comprises propylene glycol, the propylene glycol being present in an amount of "less than 5% by weight."

Prophetic Example 3 of Yu describes a "2% minoxidil" formulation formed by dissolving 2 grams minoxidil and 3 ml lactic acid into a mixture of 80 ml ethanol and 15 ml propylene glycol. A 2% minoxidil formulation contains much less minoxidil

than the present compositions which require at least 5% minoxidil. In addition, the formulation of Example 3 of Yu has a large propylene glycol content, i.e., 15%, which amount is substantially greater than the presently claimed "less than 5% by weight."

Furthermore, Applicants direct the Examiner's attention to the fact that the instant claims, i.e. claims 1 and 21, recite a pH range of from 5.0 to 7.0. In contrast, Example 3 of Yu has a pH of 4.7. Peck is silent on the issue of pH.

Thus, Applicants submit that the claimed pH is not recognized, disclosed or taught in any of the cited references as required by *In re Wilson*.

Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established. In view of the foregoing and the previously presented arguments, it is submitted that nothing in the applied references, taken alone or together, render the presently claimed subject matter obvious within the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw these rejections of claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, and 139-161.

CONCLUSION

Applicants assert that the claims are in condition for immediate allowance and early notice to that effect is earnestly solicited. Should the Examiner deem that any further action by Applicants' undersigned representative is desirable and/or necessary, the Examiner is invited to telephone the undersigned at the number set forth below.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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